PATENT SPECIFICATION

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(54) GERMICIDE

(71) We, PEROXID-CHEMIE GMBH, a body corporate of 8021. Hollriegelskreuth, Nr Munich, Federal Republic of Germany, organised and existing under the laws of the Federal Republic of Germany do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to germicides and in particular to germicidal mixtures containing hydrogen peroxide and the use of such mixtures in treating aqueous systems.

Until only recently, water has been a cheap, plentiful and natural product, but it is now becoming increasingly a valuable and expensive material which is no longer available in unlimited quantities. In consequence, attempts have been made, both in the municipal sector and in industry, to discourage as far as possible the consumption of fresh water and instead to purify and re-use water. Prior to recycling the water, it is often necessary to treat the water in one or more stages. Examples of systems which recycle water are cooling water recycled in various branches of industry, and the circulation of water in swimming pools.

In certain industries there are particular problems in recycling water, in that process water during use picks up impurities which act as nutrients for many kinds of micro-organisms. By way of example, one such industry is the paper industry, which employs mechanical separators, e.g. filters or compressors to separate the water from solids carried in the water. However, particularly in the paper industry, the water which is recovered, either from the filter or is squeezed out of the solid mass, contains cellulose, which is a very good nutrient for algae, fungi, and other bacteria. Unfortunately, even in so called closed loop processes, it is in general not economically feasible to prevent such micro-organisms entering the water system. If the micro-organisms are allowed to grow unchecked, they can appear, for example, as slime or form mould cultures, which can lead to considerable adverse effects and disturbance at some point in the water circulation system.

It has been recognised commonly that the growth of micro-organisms in water can be retarded or prevented by the addition of a suitable germicide. Various germicides have been proposed, which are effective to at last a certain extent, but which do not generate in the aqueous system disturbing toxic or corrosive by-products or reaction products. One such germicide is hydrogen peroxide which decomposes to form oxygen and water, and thus does not form any harmful residues. Now, it has been recognised that hydrogen peroxide does possess some bacteriacidal, often described as bacteristatic, deodorising, oxidising, and antiseptic properties, and also exhibits to some extent a fungistatic and fungicidal action as described in Dermatologische Wochenschrift, *152* page 1105 (1966). Although beneficial, the use of hydrogen peroxide only is sometimes only a short term solution since various micro-organisms are capable of mutating to form resistant strains which are no longer killed or significantly retarded by hydrogen peroxide. One biological clarification process, as described in DT—OS 22 28 011 describes treatment with hydrogen peroxide which meets the entire oxygen demand for the whole aerobic bacterial clarification and simultaneously prevents the development of filimentous bacteria, i.e. anaerobic bacteria. Thus, in this case, the selectively of hydrogen peroxide is utilised, demonstrating whilst certain micro-organisms are completely destroyed, at the same time the growth conditions of other micro-organisms are optimised.

Other germicidal compositions have been proposed in which hydrogen peroxide is one component. One such composition is described in DT—OS 22 21 047 in which hydrogen peroxide or a water soluble non-toxic peroxide is mixed with phenol mercury (2) salts, in particular sodium ethyl mercury thiosalicylate, and used in the form of aqueous isotonic solutions to sterilise and clean soft contact lenses. However, mercury compounds are toxic, which means that such a composition would be prohibited for use not only in swimming pools but also in industry, especially in the paper industry if the paper is intended for use in packaging food stuffs or in the pharmaceutical or food industries in which materials, which are intended for consumption or use by humans, could come into contact with toxic substances as in the recycled aqueous systems, possibly as a result of a leak from the aqueous system.

It is an object of the present invention to provide a germicidal mixture which is more effective than solely hydrogen peroxide, but which, like hydrogen peroxide, is not significantly corrosive nor is to any significant extent either toxic itself or in use produces decomposition products which are toxic.

According to the present invention there is provided a germicidal mixture comprising hydrogen peroxide and one or more of compounds:—

a) p-hydroxybenzoic acid or a salt thereof or a C_1—C_4 alkyl ester thereof,

b) a non-reactive (as herein defined) heterocyclic aromatic compound containing at least one nitrogen atom as hetero-atom and substituted by at least one hydroxyl group or carboxylic acid group or salt or C_1—C_4 alkyl ester of said acid or

c) an amidosulphonic acid having general formula RR^1NSO_3H wherein R and R^1 represent hydrogen or an C_1—C_4 alkyl group, or a salt thereof, provided that where the mixture contains one compound only of a) b) and c) and where that compound is a), it is present in an amount of not more than 0.7% and where that compound is b) it is present in an amount of at least 0.25%, %s by weight based on the mixture.

According to a second aspect of the present invention there is provided a process for the treatment of micro-organism-containing municipal or industrial water comprising the step of contacting the micro-organism-containing water with an active amount of a germicidal mixture which comprises hydrogen peroxide and one or more of compounds a), b) and c) described herein-before.

Advantageously, it has been found that the stability of the hydrogen peroxide is not impaired by the presence of the compounds a), b), or c) with the result that the shelf life of the germicidal mixture is therefore comparable with that of commercial hydrogen peroxide. Moreover, it has also been discovered that the compounds a), b), or c) display a synergistic effect when used as germicides in combination with hydrogen peroxide, in that their use jointly is considerably more effective than use of the individual components separately. The fact that synergism is exhibited is surprising and unexpected. Furthermore, it will be recognised that the compounds a), b) and c) exhibit substantially no physiologically harmful properties. This is particularly important, because it enables the germicidal mixture to be employed in disinfecting swimming pool water or for use in industry, even where water treated with the germicidal mixture is likely to come into contact through accident or design with food stuffs or pharmaceutical or packaging material for them.

When compound a), b) or c) is a salt it can suitably be an alkali metal salt, for example sodium, or it can be an ammonium salt.

In particularly desirably embodiments, compound a) of the germicidal mixture is the ethyl or propyl ester of p-hydroxybenzoic acid. The physiological harmlessness such compounds has already been recognised, in that they are permitted, for example, under the description PHB esters as preservatives in foodstuffs in at least some countries.

By the term "non-reactive" used herein with respect to compound b) we mean that the compound does not react with hydrogen peroxide. In some preferred embodiments, the heterocyclic aromatic compound is a substituted quinoline or pyridine. More preferably, the compound b) is an hydroxyquinoline or a pyridinedicarboxylic acid. Particularly preferred compounds include 8-hydroxyquinoline and dipicolinic acid.

Although in compound c) of the germicidal mixture, the groups R and R^1 in the general formula can be C_1—C_4 alkyl groups, such as methyl or ethyl, in highly convenient embodiments, R and R^1 are both hydrogen.

Generally, the germicidal mixture contains water in addition to the hydrogen peroxide and one or more of the compounds a), b) and c). In preferred embodiments, the water contains in addition a small amount of a mineral acid, for example sulphuric acid. Other mineral acids which are physiologically acceptable in small amounts

may be included instead of sulphuric acid. Advantageously, the addition of a small amount of mineral acid enables compounds from compounds a) b) and c) which exhibit comparatively poor solubility in water to be dissolved more readily.

The concentration of hydrogen peroxide in the germicidal mixture will often fall in the range of 10 to 70% by weight, and frequently within the range of 30 to 50% by weight. The concentration of the compound a), b), or c) in the germicidal mixture is usually within the range of 0.1 to 5% by weight. The weight ratio of hydrogen peroxide to compound a) in the germicidal mixture is often in the range of 250:1 to 100:1, and the weight ratio of hydrogen peroxide to either compound b) or compound c) is often in the range of 25:1 to 10:1.

Conveniently, the germicidal mixtures described herein in some embodiments can be obtained by adding the appropriate amount of compound a), b) or c) to commercially available aqueous solutions of hydrogen peroxide. Such commercially available solutions can contain the normal stabilising agents for hydrogen peroxide, such as sodium pyrophosphates, because such stabilising agents do not markedly impair the synergistic effect, nor do they interact with the compounds a), b) or c) added thereto.

In processes for treating water with the germicidal mixtures, it is highly desirable to use from 0.001 to 2 ml of mixture per litre of water to be treated, calculated on the content of 35% by weight hydrogen peroxide in the germicidal mixture. Thus, e.g., if the germicidal mixture contained approximately 50% by weight hydrogen peroxide, the corresponding amount would be approximately 0.007 to 1.4 ml per litre of water. Such amounts are particularly suitable for the treatment of water supplies containing a significant amount of dissolved nutrient for micro-organisms, such as cellulose or hydrolysis products thereof.

Many aqueous systems often contain chambers, pumps, connecting pipes, and the like which are liable to corrosion, to at least some extent. If desired, the germicidal mixture can contain a corrosion inhibitor commonly incorporated in hydrogen peroxide solutions, such as ammonium nitrate. Such a compound can be incorporated without significantly impairing the synergistic effect between the hydrogen peroxide and the compounds a), b) or c).

Aqueous medium can be treated with the germicidal mixture by any conventional apparatus for bringing one liquid into contact with a second liquid. Thus, for example, the germicidal mixture can be added continuously or intermittently, and, for example, can be injected or pumped into the pipeline carrying the recycled water or be added in a sparate treatment vessel.

Having now described the invention generally, specific embodiments will now be described more fully by way of example only.

Examples 1—7.

In these Examples, germicidal mixtures were prepared by mixing aqueous hydrogen peroxide with one or more of compounds a) to c) in the appropriate amounts to give the product compositions specified in Table I below. In all the examples, the balance was made up with water. Where sulphuric acid was incorporated, it represented the minimum amount to allow the complete solution of the hydroxyquinoline compound. In Examples 1—7, concentrations are weight percent, unless otherwise stated.

TABLE I

Example No.	Hydrogen Peroxide Conc n	Other Components	
		Compound	Conc n
1	35	ammonium amidosulphonate	2
2	35	p-hydroxybenzoic acid-ethyl ester	0.13
3	35	dipicolinic acid	0.5
4	35	ammonium amidosulphonate	2
		sodium pyrophosphate	0.5
5	35	ammonium amidosulphonate	2
		dipicolinic acid	0.25
6	35	8-hydroxyquinoline	2
		dipicolinic acid	0.25
		sulphuric acid	Min.
7	35	8-hydroxyquinoline	2
		p-hydroxybenzoic acid-ethyl ester	0.13
		sulphuric acid	Min.

The germicidal mixtures described in Table I were storage stable and retained their effectiveness for a considerable period of time.

Examples 8—14 and Comparisons.

In these Examples and comparisons, the effectiveness of the germicidal mixtures of Examples 1—7 was determined and compared with treatments employing one or other of the components of the germicidal mixture or with a blank. The solutions which were treated by the germicidal mixtures were prepared by treating a Dubo's salt solution comprising 0.5 g $NaNO_3$ 1 g Na_2HPO_4, 0.5 g $MgSO_4.7H_2O$, 0.5 g KCl, 0.01 g $SO_4.7H_2O$ and 1 litre distilled water with 5 g cellulose powder, 0.1 g yeast extract and 5 g humic soil and aerated for several weeks. The cellulose containing solution was then diluted to approximately 10% concentration with fresh Dubo's salt solution. In each one, a sample of the diluted cellulose containing solution was treated with the amount of germicidal mixture indicated in Table II, and incubated at 15°C with slight aeration. The bacteria count was measured using PC agar, incubating for 10 days at 22°C, measurements being made initially and after 1, 7, 14, and 20 days. For purposes of comparison only, blank tests were conducted, i.e. without the addition of any germicide, as well as tests under identical conditions but employing a germicidal mixture containing no hydrogen peroxide, but otherwise identical to the mixture used in the corresponding example. Tests run employing solely hydrogen peroxide as a germicide were carried out. The results of the tests are summarised in Table II. The number of living bacteria stated in the Table is the number contained per one ml of the diluted cellulose solution employed in the test. The term "NT" indicates that no living bacteria were detected in the 0.1 ml batch. Comparisons are indicated by the prefix C, and where they carry the same numeral as an Example, then that comparison is identical to the example except for the omission of hydrogen peroxide.

TABLE 2

Example No.	Germicidal Mixture	Conc^{n} of Mixture (ml/l)	Bacteria Count				
			Initial	1 day	7 days	14 days	21 days
8	Ex. 1	0.25	2×10^{4}	NT	NT	NT	–
C8	C 1		2×10^{5}	4×10^{5}	3×10^{7}	5×10^{5}	–
9	Ex. 2		2×10^{4}	NT	NT	NT	–
C9	C 2		2×10^{5}	2×10^{6}	3×10^{6}	10^{6}	–
10	Ex. 3		2×10^{5}	NT	NT	NT	–
C10	C 3		2×10^{5}	2×10^{6}	5×10^{5}	10^{8}	–
11	Ex. 4		5×10^{5}	NT	NT	NT	–
C11	C 4		2×10^{6}	3×10^{8}	4×10^{5}	5×10^{5}	–
12	Ex. 5	0.05	3×10^{8}	2×10^{3}	NT	–	NT
C12	C 5		3×10^{8}	1×10^{8}	8×10^{6}	–	3×10^{6}
13	Ex. 6		3×10^{8}	6×10^{2}	NT	–	NT
C13	C 6		3×10^{8}	1×10^{8}	10^{6}	–	10^{6}
14	Ex. 7		3×10^{8}	3×10^{2}	NT	–	NT
C14	C 7		3×10^{8}	1×10^{8}	3×10^{7}	–	2×10^{6}
C15	–	–	7×10^{4}	6×10^{5}	5×10^{6}	2×10^{6}	–
C16	H_2O_2	0.25	5×10^{4}	2×10^{2}	5×10^{1}	5×10^{2}	–
C17	–	–	3×10^{8}	3×10^{8}	8×10^{6}	–	1×10^{7}
C18	H_2O_2	0.25	3×10^{8}	10^{6}	10^{3}	–	2×10^{4}

From Table II it can be seen that when the germicidal mixture was used in a concentration of 0.25 ml/l, in every case the bacteria count fell to an unmeasurable level within one day, whereas at best the comparison with the hydrogen peroxide-free mixtures caused only a slight and initial decrease in the bacteria. Use of hydrogen peroxide by itself at that concentration did produce a decrease in the bacteria count, but it was much more slowly and it will be noted that after 14 days the bacteria count had risen to higher than that measured after one day. This indicates that the germicidal compound had not been sufficiently active to reduce the bacteria to a nil level, and that the bacteria were then multiplying again. A similar pattern occurred when the concentration of the germicidal mixture was reduced to only 0.05 ml/l. As would be expected when the concentration of germicidal mixture is reduced by five times, its action was slower, but even then had reduced the bacteria count to unmeasurable levels within seven days, from a significantly higher initial bacteria count. Once again the germicidal mixture of the examples demonstrated far superior germicidal properties than any of the comparison mixtures or hydrogen peroxide by

itself. Moreover, it will be observed that the improvement of the mixture over its components is signficantly greater than the additive effects of the individual components, indicating clearly synergism. Furthermore, it will be noted that the presence of a normal stabiliser for H_2O_2, as in example 4, or small quantities of mineral acid, as in Examples 6 and 7 do not destroy the synergism.

Example 15.

In this Example, a gemicidal mixture comprising 35% w/w hydrogen peroxide and the ethyl ester of p-hydroxybenzoic acid in a sugar beet process initially at a concentration of 3 ppm mixture to cure the problem of slime, especially in the cooling tower. When the slime had been eliminated, the dosage was lowered to 1.5 ppm of mixture without the slime reappearing.

WHAT WE CLAIM IS:—

1. A germicidal mixture comprising hydrogen peroxide and one or more of compounds:—

a) p-hydroxybenzoic acid or a salt thereof or a C_1—C_4 alkyl ester thereof,

b) a non-reactive (as herein defined) heterocyclic aromatic compound containing at least one nitrogen atom as hetero-atom and substituted by at least one hydroxyl group or carboxylic acid group or salt or C_1—C_4 alkyl ester of said acid or

c) an amidosulphonic acid having general formula RR^1NSO_3H wherein R and R^1 represent hydrogen or an C_1—C_6 alkyl group, or a salt thereof, provided that where the mixture contains one compound only of a) b) and c) and where that compound is a), it is present in an amount of not more than 0.7% and where that compound is b) it is present in an amount of at least 0.25%, %s weight by based on the mixture.

2. A germicidal mixture as claimed in claim 1 containing in addition a small amount of mineral acid.

3. A germicidal mixture as claimed in claim 2 wherein the mineral acid is sulphuric acid.

4. A germicidal mixture as claimed in any preceding claim wherein compound a), b) or c) is selected within the range of 0.1 to 5% by weight.

5. A germicidal mixture as claimed in any preceding claim wherein compound a) is present in a weight ratio to hydrogen peroxide of from 1 to 250 to 1 to 100.

6. A germicidal mixture as claimed in any preceding claim wherein the concentration of hydrogen peroxide is in the range of 30 to 50% by weight and of compound a) is not more than 0.5% by weight.

7. A germicidal mixture as claimed in any preceding claim wherein compound a) is the ethyl or propyl ester of p-hydroxybenzoic acid.

8. A germicidal mixture as claimed in any of claims 1—4 wherein compound b) or c) is present in a weight ratio to the hydrogen peroxide of from 1 to 25 to 1 to 10.

9. A germicidal mixture as claimed in any of claims 1—4 or 8 wherein the heterocyclic compound b) contains only one nitrogen atom in the aromatic nucleus.

10. A germicidal mixture as claimed in claim 9 wherein the compound b) is an hydroxyquinoline or a pyridine dicarboxylic acid.

11. A germicidal mixture as claimed in claim 10 wherein compound b) is 8-hydroxyquinoline or dipicolinic acid.

12. A germicidal mixture as claimed in any of claims 1—4 or 8 wherein compound c) is an ammonium salt.

13. A germicidal mixture as claimed in any preceding claim which is formed by mixing commercially available aqueous hydrogen peroxide, containing if desired, conventionally used stabilisers, with one or more of compounds a), b) or c) in the desired weight ratio.

14. A germicidal mixture as claimed in any preceding claim containing additionally a corrosion inhibitor.

15. A germicidal mixture substantially as described herein with respect specifically to any one of Examples 1—7.

16. A process for the treatment of micro-organism-containing municipal or industrial water comprising the step of contacting the micro-organism-containing water with an active amount of a germicidal mixture which comprises hydrogen peroxide and one or more of compounds:—

a) p-hydroxybenzoic acid or a salt thereof or a C_1—C_4 alkyl ester thereof,

b) a non-reactive heterocyclic aromatic compound containing at least one nitrogen atom as hetero-atom and substituted by at least one hydroxyl group or at least one acid group or salt or C_1—C_4 alkyl ester of the acid group, or

c) an amidosulphonic acid having general formula RR^1NSO_3H wherein R and R^1 represent hydrogen or an C_1—C_6 alkyl group, or salt thereof.

17. A process as claimed in claim 16 employing a mixture according to any of claims 2 to 15.

18. A process as claimed in claim 16 or 17 wherein the treated water is likely to come into contact with humans by design, leakage, or otherwise without being treated with other germicidal compounds.

19. A process as claimed in any of claims 16 to 18 wherein the industrial water is recycle water or effluent.

20. A process as claimed in any of claims 16 to 19 wherein the industrial water is washing, process or cooling water.

21. A process as claimed in claim 18 wherein the municipal water is used in swimming pools.

22. A process as claimed in any of claims 15 to 21 wherein the water contains cellulose or an hydrolysis derivative thereof as nutrient for micro-organisms.

23. A process as claimed in claim 22 wherein the water is water separated from aqueous paper pulp.

24. A process as claimed in any of claims 16 to 23 wherein the germicidal mixture is employed in an amount of from 0.001 to 2 ml per litre of water, calculated on the basis of a hydrogen peroxide content of 35% by weight.

25. A process as claimed in any of claims 16 to 24 wherein the germicidal mixture employed is a preformed mixture containing hydrogen peroxide and one or more of the compounds a, b), and c) in the desired weight ratio for the treatment of the water.

26. A process for treating water with a germicidal mixture, substantially as described herein with respect specifically to any of Examples 8 to 14.

27. Water whenever treated by a process as claimed in any claims 16 to 26.

T. PEARCE,
Agent for the Applicants.

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